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PATREA L. PABST
HOLLAND & KNIGHT LLP
SUITE 2000, ONE ATLANTIC CENTER
1201 WEST PEACHTREE STREET, N.E.
ATLANTA, GA 30309-3400

EXAMINER	
SEAMAN, D MARGARET M	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 33

Application Number: 09/506,988
Filing Date: February 18, 2000
Appellant(s): TANG ET AL.

Todd Hofmeister
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1 May 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

Claims 5 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This appeal involves claims 1, 2, 4, 6-8, 10 and 12, rejected under 35 USC §112, first paragraph enablement and written description and claims 1, 2, 4, 6-8, 10 and 12 rejected under 35 USC §102(b).

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: Claims 1, 2, 4, 6-8, 10 and 12 are rejected (1) under 35 USC § 112, first paragraph (lack of enablement), (2) under 35 USC § 112, first paragraph (written description) and (3) under 35 USC § 102(b) (Jadhav, US Patents #5,491,149 & #5,683,999).

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1, 2, 4-8 and 10-12 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,491,149	Jadhav 2	02-1996
5,683,999	Jadhav 1	11-1997

For the above reasons, it is believed that the rejections should be sustained.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The rejection of claims 1, 2, 4, 6-8, 10 and 12 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, as stated in paper #22, dated 17 December 2001, is upheld.

As previously stated, there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any

necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims: The claims appear to encompass all compounds having two or more of two atoms in conformation (isosteres) that mimic the transition state of aspartic acid protease.

The nature of the invention: The nature of the intention is aspartic acid protease inhibitors that are used to treat patients in need of such aspartic acid protease inhibition.

The state of the prior art: The prior art has several compounds such as saquinavir, indinavir and ritonavir that have single transition-state isostere.

The level of predictability in the art: The level of predictability in the art is hard to describe when there is only one compound presented in the instant application that has two or more transition-state isosteres, namely compound identified as UIC-98-056.

The amount of direction provided by the inventor: There is little direction provided by the inventor due to the ambiguousness of the definition of

"transition-state isostere" presented on page 3 line 26 of the instant application. The only working example is the one compound UIC-98-056. The only direction given for the identity of the isosteres that are effective in aspartic acid protease inhibitors are hydroxyethylene, dihydroxyethylene, hydroxyethylamine, phosphinate and reduced amide. No other examples are given and no direction is provided by the inventor in the instant application as to what would be the next direction to go in which to seek other active compounds.

The existence of working examples: There is only one working example of a two transition-state isostere, UIC-98-056.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The quantity of experimentation needed to make the instant invention is undue due to the lack of direction provided by applicants.

Taking the above factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make or use the instant invention, other than the one compound, identified as UIC-98-056.

3. The rejection of claims 1, 2, 4, 6-8, 10 and 12 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. It is not seen where the instant specification describes the instant invention such that the ordinary artisan could make or use the instant invention, as stated in paper #22, is upheld.

Specifically, the only description of a "transition-state isostere" in the specification is on page 3 line 26 and the only examples are on page 4 lines 4-6. A transition-state isostere is a compound wherein two carbon atoms in tetrahedral conformation mimic the transition state of catalysis. Not all of the examples have two carbon atoms in tetrahedral conformation. The specification shows only one compound, identified as UIC-98-056, having two such transition-state isosteres. There are no other examples of other carbon atoms in tetrahedral conformation that fit this definition. The specification fails to provide description for the scope of different compounds to be incorporated into the large and structurally diverse compounds that potentially might fit this definition. The size, shape, and conformation which is dependent upon the therapeutic agent is considered critical to the practice of the presently claimed compounds/methods since such parameters have been demonstrated to be critical for obtaining efficacy (e.g. drug delivery). See Ex Parte Bhide (Bd Pat. App. & Int.) 42 USPQ2d 1441 (e.g. critical core structure necessary for biological activity must be present in the claimed invention). The prior art clearly demonstrates the criticality of the choice of compound, the amount or compound and the conditions (e.g. pH, temperature, administration time in

order to achieve effective inhibition of protease) to incorporate compounds that are large in size and/or which differ in physical/chemical properties. This criticality results from the unpredictability of the compound in binding to the protease, which differs from compound to compound, and which are stereospecific with respect to the compound. Due to this, it is not seen where the instant specification adequately describes the instant invention.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 4, 6-8, 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Jadhav (US Patent #5,491,149 and #5,683,999).

Jadhav discloses compounds that are aspartic acid protease inhibitors that are inhibitors of HIV (see column 2 lines 15-16 and 40). These compounds have two or more isosteres as described on page 4 of the instant specification that mimic the transition state of aspartic acid protease. The first compound is column 38 of '999 wherein Q is NH. The second compound is column 67

example 70. Jadhav also discloses compounds having these two or more isosteres in the '149 patent. Column 47 examples 52, 56 and 57. Column 49 example 26. Column 51 examples 19 and 20. Column 55 examples 16, 20 and 21. Column 57 examples 2, 3, 50 and 51. Column 61 examples 43, 47 and 48. Column 63 example 29.

Claim Objections

1. Claims 5 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

(11) Response to Argument

First, Applicant argues on page 9 that the similarity of the core structure of the aspartyl proteases drives the common mechanistic features of enzymatic cleavage of proteins and polyprotein bonds within this class of proteins. The studies that detail the structural core of the HIV protease and other aspartyl proteases are outlined in the specification.

However, it is the Examiner's position that the structural core of aspartyl proteases are not being claimed. Due to this, it doesn't matter what studies of these structural catalytic cores show or do not show. What is being claimed are compounds that inhibit

this protease and therefore treat certain medical conditions. The core of these compounds that are being claimed have not been disclosed by Applicants.

Second, Applicant argues designing an inhibitor relies of this essential information because it is the activity of the core of the protease that is being inhibited. Once the core structure and/or catalytic mechanism has been elucidated, the design and construction of an inhibitor harboring two or more isosteres can be accomplished without undue experimentation, as provided for in the presently claimed invention.
However, it is the Examiner's position that Applicant has given conceptual framework as to how to discover compounds that have the possibility to inhibit aspartic proteases. The instant claims are drawn to a compound and methods of treating using a compound. However, this structural framework is not a Markush of compounds and does not enable the treatment of conditions. The instant specification has not shown that Applicant has possession any compounds other than the compound of claims 5 and 11, that inhibits aspartic protease.

Third, Applicant argues that they have provided examples and description of isostere harboring aspartyl protease inhibitors.
However, it is the Examiner's position that the examples of compounds having isostere harboring aspartyl protease inhibitors have only one isostere (as applicant has defined it) and are fully known and commercially available compounds such as saquinavir,

indinavir and ritonavir. As applicant has described these compounds, they have only one isostere. The only example of a compound that has two or more isosteres is the compound identified as UIC-98-056 of claims 5 and 11. There are no other examples of other compounds having two or more isosteres. There is no Markush of compounds that have two or more isosteres. According to Applicant, the standard modes of administration and their formulation is correct for compounds having one isostere. Applicant has not provided a nexus between the formulation and administration between compounds having one isostere and compounds having two or more isosteres.

Fourth, Applicant argues that it would not require undue experimentation based upon the appellant's disclosed detailed method of making and testing the two isostere inhibitor and the structural characterization of the cores of aspartyl proteases, from which the presently claimed invention relies upon.

However, it is the Examiner's position that the detailed method of making the compounds having two or more isosteres is not detailed with respect to compounds other than UIC-98-056. Only this one compound having two or more isosteres has been made and tested. The detailed studies of the structural characterization of the cores of aspartyl proteases is not being claimed.

Fifth, Applicant argues that in *Enzo II,* the written description requirement can be met by a functional description of claimed materials if coupled with a known or disclosed correlation between function and structure.

However, it is the Examiner's position that while a functional description of what a compound needs to inhibit to treat conditions has been provided, this has not been coupled with a disclosed structure other than a compound having two or more isosteres. This is not a structure of a group of compounds. This correlation of two or more isosteres has not been fully correlated to the inhibition of aspartic protease because the known compounds of saquinavir, indinavir and ritonavir have only one isostere.

Sixth, Applicant argues that an example of a transition state isostere has been given. However, this example of a transition state isostere is a mere fragment and not a full structure of a compound that fulfills the instant claims.

Seventh, Applicant argues that Jadhav 1 fails to contemplate two or more transition state isosteres in a polypeptide backbone.

However, it is the Examiner's position that even though Jadhav does not specifically state that the compounds taught have two or more transition state isosteres in a polypeptide backbone, the compounds taught do fall within the scope of the instantly claimed invention by having these two or more isosteres. The compounds taught by

Jadhav 1 inhibit aspartic acid protease and inhibit HIV protease (see column 2 lines 15-16 and 40 of Jadhav 1). These compounds have two or more isosteres as described on the instant specification's page 4. The compounds of Jadhav 1 meet all the requirements for the instant claims.

Eighth, Applicant argues that Jadhav 2 fails to contemplate two or more transition state isosteres.

However, it is the Examiner's position, as stated above in the reply to the seventh argument, that the requirement for a rejection under 35 USC §102(b) that the specifics of the claims must be met. The compounds taught by Jadhav 2 contain fragments that have been identified by applicant's own specification as being isosteres. The compounds have two or more of these fragments. The compounds of Jadhav 2 inhibit aspartic protease and inhibit HIV protease, as is instantly claimed. This meets the requirements for rejection under 35 USC §102(b).

Ninth, Applicant argues that the Examiner has not individually examined the dependent claims.

However, it is the Examiner's position that all of the dependent claims have been examined due to the fact that the dependent claims have been either rejected under 35 USC §112, first paragraph (written description and lack of enablement) and/or 35 USC §102(b) or they have been objected.

Tenth, Applicant argues that claims 2, 6, 8 and 12, wherein the specific formula of the isostere is substituted with two other isosteres, has not been addressed.

However, it is the Examiner's position that claims 2 and 8 do not have this limitation of being substituted with a specific isostere and two other isosteres. Claims 6 and 12 do not state which are the other isosteres are in addition to the one specified in the claims. The definition of isosteres that are encompassed by the instant invention does not state all of the isosteres. The definition states that the isosteres "include" the following fragments. Due to this, Applicant has not stated that the rest of the compounds taught by Jadhav are not encompassed by "isosteres" as defined by the instant invention.

Eleventh, Applicant argues that claims 3 and 10 have not been addressed as to why they are not definite and enabled.

However, it is the Examiner's position that claim 3 has been deleted by Applicant and is not part of any rejection. Claim 10 falls within the rejection of claims as lacking written description and enablement under 35 USC §112, first paragraph and under 35 USC §102(b) as stated in the above rejections.

Twelfth, Applicant argues that claims 5 and 11 have been enabled but is rejected under 35 USC §112, first paragraph.

However, it is the Examiner's position that claims 5 and 11 have not been rejected under 35 USC §112, first paragraph and they are objected to as being dependent upon a

rejected base claim and would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Thirteenth, Applicant argues that the examiner is relying on conclusionary statements without putting forth specific reasons describing why the claims are not enabled by the specification.

However, it is the Examiner's position that such specific reasons have been provided in the rejections under 35 USC §112, first paragraph for written description and enablement (see the re-stated rejections in the above section (10)). This section contains the original statements and arguments as to why the claims lack written description and enablement.

Respectfully submitted,

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms
September 17, 2003

Conferees

ZINNA NORTHINGTON DAVIS
PRIMARY EXAMINER

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Patrea L Pabst
Arnall Golden & Gregory LLP
2800 One Atlantic Center
1201 West Peachtree Street
Atlanta, GA 30309-3450